Claims

What is claimed is:

1. An array comprising spots of at least one type of protein attached to a solid support, wherein the density of said array of proteins is at least 1000 spots per cm^2.

2. The array of claim 1, wherein the proteins are functional.

3. The array of claim 1, wherein a substantial fraction of the proteins are functional.

3. The array of claim 1, wherein the array comprises proteins that are properly folded into their natural conformation.

4. The array of claim 1, wherein the density of the array is at least 1500 spots per cm^2.

5. The array of claim 1, wherein the proteins are attached to the solid support through a non-covalent interaction.

6. The array of claim 1, wherein the proteins are attached to the solid support through a covalent interaction.

7. The array of claim 5 or 6, wherein said interaction is characterized in that the linkage is robust enough so that the compounds are (1) not inadvertently cleaved during subsequent manipulation steps and (2) inert so that the functionalities employed do not interfere with subsequent manipulation steps.

8. The array of claim 5 or 6, whereby the interaction results in a substantial fraction of the arrayed proteins being functional.

9. The array of claim 6, wherein the covalent interaction is a Schiff's base linkage.

10. The array of claim 6, wherein the covalent interaction is generated by a transacylation reaction between the protein and a chemical moiety on the solid support.

11. The array of claim 6, wherein the covalent interaction is generated by a Michael addition reaction.

12. The array of claim 6, wherein the covalent interaction is a disulfide bond.

13. The array of claim 5, wherein the non-covalent interaction is an epitope-antibody interaction.

14. The array of claim 5, wherein the non-covalent interaction is a poly-histidine-metal cation interaction.

15. The array of claim 5, wherein the non-covalent interaction is nonspecific.

16. The array of claim 5 or 6, wherein the interaction between the protein and the solid support occurs through an interaction with a non-natural polymeric matrix.

17. The array of claim 16, wherein the polymeric matrix is dextran.

18. The array of claim 16, wherein the matrix is less than 500 nm thick.

19. The array of claim 1, wherein the space between the spots of the array is occupied by a blocking agent.

20. The array of claim 19, wherein the blocking agent is a protein.

21. The array of claim 19, wherein the blocking agent is selected from the group consisting of bovine serum albumin, caseine, and nonfat milk.

22. The array of claim 19, wherein the blocking agent is a small molecule.

23. The array of claim 19, wherein the blocking agent is selected from the group consisting of glycine, ethanolamine, and ethylenediamine.

24. The array of claim 1, wherein the solid support is glass.

25. The array of claim 1, wherein the solid support is a polymer.

26. The array of claim 1, wherein the solid support comprises a metal surface.

27. The array of claim 1, wherein the solid support comprises a self-assembled monolayer.

28. An array comprising spots of at least one type of protein attached to bovine serum albumin (BSA) coated onto a solid support, wherein the density of said array of proteins is at least 1000 spots per cm^2.

29. The array of claim 28, wherein the proteins are functional.

30. The array of claim 28, wherein a substantial fraction of the proteins are functional.

31. The array of claim 28, wherein the array comprises proteins that are properly folded into their natural conformation.

32. The array of claim 28, wherein the density of the array is at least 1500 spots per cm^2.

33. The array of claim 28, wherein the proteins are attached to the BSA through a non-covalent interaction.

34. The array of claim 28, wherein the proteins are attached to the BSA through a covalent interaction.

35. The array of claim 33 or 34, wherein said interaction is characterized in that the linkage is robust enough so that the compounds are (1) not inadvertently cleaved during subsequent manipulation steps and (2) inert so that the functionalities employed do not interfere with subsequent manipulation steps.

36. The array of claim 33 or 34, whereby the interaction results in a substantial fraction of the arrayed proteins being functional.

37. The array of claim 34, wherein the covalent interaction is a Schiff's base linkage.

38. The array of claim 34, wherein the covalent interaction is generated by a transacylation reaction between the protein and a chemical moiety on the BSA.

39. The array of claim 34, wherein the covalent interaction is generated by a Michael addition.

40. The array of claim 34, wherein the covalent interaction is a disulfide bond.

41. The array of claim 33, wherein the non-covalent interaction is an epitope-antibody interaction.

42. The array of claim 33, wherein the non-covalent interaction is a poly-histidine-metal cation interaction.

43. The array of claim 33, wherein the non-covalent interaction is nonspecific.

44. The array of claim 28, wherein the solid support is glass.

45. The array of claim 28, wherein the solid support is a polymer.

46. The array of claim 28, wherein the solid support comprises a metal surface.

47. The array of claim 28, wherein the solid support comprises a self-assembled monolayer.

48. A method of preparing an array of proteins, the method comprising the steps of:

providing a solid support, wherein the solid support is functionalized with a chemical moiety capable of interacting with a protein;

providing one or more solutions of one or more types of proteins to be attached to the solid support; and

delivering said one or more solutions to the solid support, whereby each of the proteins is attached to the solid support through an interaction, and whereby the array of proteins has a density of at least 1000 spots per cm^2.

49. The method of claim 48, wherein the solid support is glass.

50. The method of claim 48, wherein the solid support is a polymer.

51. The method of claim 48, wherein the solid support comprises a metal surface.

52. The method of claim 48, wherein the solid support comprises a self-assembled monolayer.

53. The method of claim 48, wherein the proteins attached to the array are functional.

54. The method of claim 48, wherein the linkage is a covalent interaction.

55. The method of claim 48, wherein the linkage is a non-covalent interaction.

56. The method of claim 48, wherein the density is at least 1500 spots per cm^2.

57. The method of claim 48, further comprising the step of blocking unoccupied sites on the solid support with a blocking agent.

58. The method of claim 57, wherein the blocking agent is selected from the group consisting of bovine serum albumin (BSA), caseine, nonfat milk, glycine, ethylenediamine, and ethanolamine.

59. The method of claim 48, wherein the solid support comprises a polymer functionalized with chemically activated groups.

60. The method of claim 48, wherein the solutions are aqueous solutions.

61. A method of preparing an array of proteins, the method comprising steps of:

providing a solid support, wherein the solid support is coated with bovine serum albumin (BSA) functionalized with a chemical moiety capable of interacting with a protein;

providing one or more solutions of one or more types of proteins to be attached to the solid support; and

delivering said one or more solutions to the solid support, whereby each of the proteins is attached to the solid support through a covalent interaction, and whereby the array of proteins has a density of at least 1000 spots per cm^2.

62. The method of claim 61, wherein the solid support is glass.

63. The method of claim 61, wherein the solid support is a polymer.

64. The method of claim 61, wherein the solid support comprises a metal surface.

65. The method of claim 61, wherein the solid support comprises a self-assembled monolayer.

66. The method of claim 61, wherein a substantial fraction of the proteins are functional.

67. The method of claim 61, wherein the interaction is a covalent interaction.

68. The method of claim 61, wherein the interaction is a non-covalent interaction.

69. The method of claim 61, wherein the density is at least 1500 spots per cm^2.

70. The method of claim 61, wherein the solutions are aqueous solutions.

71. A method of determining the interaction of protein with a molecule of interest, the method comprising the steps of:

providing an array of one or more types of proteins, wherein the array of proteins has a density of at least 1000 spots per cm^2;

contacting the array with one or more types of molecules of interest; and

determining the interaction of specific protein-molecule partners.

72. The method of claim 71, wherein the molecule of interest is a biological macromolecule.

73. The method of claim 72, wherein the biological macromolecule is a protein.

74. The method of claim 73, wherein the biological macromolecule is a protein kinase.

75. The method of claim 73, wherein the biological macromolecule is an antibody.

76. The method of claim 72, wherein the biological macromolecule is a nucleic acid.

77. The method of claim 71, wherein the molecule of interest is a small molecule.

78. The method of claim 71, wherein the array comprises a solid support of glass.

79. The method of claim 71, wherein the array comprises an array of functional proteins.

80. The method of claim 71, wherein the array comprises an array of proteins covalently attached to a solid support.

81. The method of claim 71, wherein the interaction is an enzyme-substrate interaction.

82. A method of determining the interaction of protein with a molecule of interest, the method comprising the steps of:

providing an array of one or more types of proteins, wherein the proteims are attached to bovine serum albumin attached to a solid support, and wherein the array of proteins has a density of at least 1000 spots per cm^2;

contacting the array with one or more types of molecules of interest; and

determining the interaction of specific protein-molecule partners.

83. The method of claim 82, wherein the molecule of interest is a biological macromolecule.

84. The method of claim ~~83,~~ wherein the biological macromolecule is a protein.

85. The method of claim 84, wherein the biological macromolecule is a protein kinase.

86. The method of claim 84, wherein the biological macromolecule is an antibody.

87. The method of claim 83, wherein the biological macromolecule is a nucleic acid.

88. The method of claim 82, wherein the molecule of interest is a small molecule.

89. The method of claim 82, wherein the array comprises a solid support of glass.

90. The method of claim 82, wherein the array comprises an array of functional proteins.

91. The method of claim 82, wherein the array comprises an array of proteins covalently attached to BSA attached to a solid support.

92. The method of claim 82, wherein the interaction is an enzyme-substrate interaction.

93. A method for identifying molecules able to compete with a ligand for binding to a chemical compound, the method comprising steps of:

providing a solid support coated with a chemical compound;

contacting the solid support with a ligand known to bind to the chemical compound;

contacting the solid support with a molecule to be screened for its ability to compete with the known ligand for binding to the chemical compound; and

determining loss of the ligand known to bind to the chemical compound.

94. The method of claim 93 wherein the chemical compound is selected from the group consisting of proteins, peptides, polynucleotides, small molecules, carbohydrates, and lipids.

95. The method of claim 93 wherein the molecule to be screened is selected from the group consisting of peptides, proteins, small molecules, carbohydrates, lipids, and polynucleotides.

96. The method of claim 93 wherein the molecule to be screened is labeled with a fluorophore.

97. The method of claim 93 wherein the ligand is selected from the group consisting of peptides, proteins, small molecules, carbohydrates, lipids, and polynucleotides.

98. The method of claim 93 wherein the ligand is labeled with a fluorophore.

99. The method of claim 93 wherein the step of determining comprises detecting fluorescence of the labeled ligand.

100. The method of claim 93, wherein the chemical compound is a protein, and wherein the ligand is a peptide.

101. The method of claim 93, wherein the chemical compound is a protein, and wherein the ligand is a small molecule.

102. The method of claim 93, wherein the chemical compound is a protein receptor.

103. The method of claim 93, wherein the step of contacting with a ligand comprises arraying the ligand onto the coated solid support.

104. The method of claim 93, wherein the step of contacting the solid support with a molecule comprises arraying the molecule onto the coated solid support.